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EXAMINER	
CORNET, JEAN P	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
06/03/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,200	SPRINGER ET AL.	
	Examiner	Art Unit	
	JEAN CORNET	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-15* is/are pending in the application.

4a) Of the above claim(s) *14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-13 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/24/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application for patent entered the national stage in the United States of America under 35 USC 371 from PCT/IL03/00552, filed 07/03/2003, claiming benefit from application no. 150906, filed 07/25/2002. Claims 1-7 are canceled as per applicant. Claims 8-15 are pending.

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. All claims receive the benefit of said application no. 150906, filing date: 07/25/2002

Information Disclosure Statement

3. All references submitted on the IDS dated 01/24/2005 have been considered, except where no copy is provided.

Election/Restrictions

4. Claim14 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 03/26/2009.

Applicant's election with traverse of Group I, claims 8-15 in the reply filed on 03/26/2009 is acknowledged. The traversal is on the ground(s) that the US Patent 5,205,290 (Unger et al.) does not disclose microspheres of size in the range of about 0.1-10 microns and is silent about the use of biodegradable polymeric microspheres for detecting pulmonary aspiration or gastroesophagal reflux, rather focusing on the use of the disclosed microspheres to improve computed tomography images of the gastrointestinal tract, thus the claims are novel under the unity of invention. Furthermore, claims 14 of Group II is drawn to a product that includes the novel microspheres possess unity of invention. Thus, claim 14 also possesses unity under the applicable standards. Applicants urge the PTO to reconsider and withdraw the restriction requirement

The use claim 15 is improper under 35 USC 101, see 101, rejection below, as it can be interpreted as being directed to a method of use or a product as well as a method of making the product, therefore a new lack of unity is set forth below.

The special technical feature of Group I-II is obviated by the 103 rejection outlined below; the technical feature linking the invention of Group I and II does not constitute a special technical feature as defined by PCT Rule 13.2 as it does not define a contribution over the prior art. Accordingly Groups I and II are not so linked by the same and corresponding special technical feature as to form a single invention concept. In addition, the species are deemed to lack unity of invention as well because they are not so linked as to form a single generative concept under PCT Rule 13.1. as the

species lacks inventive step. In addition, the request to withdrawn the restriction requirement is denied, because unity is still lacking among the Groups as stated in the statement above.

Claims 8-13 and 15 are currently under examination on the merit.

Specification

5. The disclosure is objected to because of the following informalities: there is a typo on page 6, sixth paragraph of the specification. "poylactic" should be polylactic.

Appropriate correction is required.

Claim Rejections – 35 USC 112 2nd Paragraph / 35 U.S.C. 101

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 15 is rejected under 35 USC 112 second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as their invention, and, under 35 U.S.C. 101, for falling to within any of the defined statutory classes of patentable subject matter.

Claim 15 is a "use claim." Claim 15 provides for the "[u]se of biodegradable microspheres having a diameter of about 0.1-10 microns for the manufacture of a diagnostic composition for detecting pulmonary aspiration", but, since the claim does not set forth any steps involved in the purported method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Claim 15 is also rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in a purported method/process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example Ex parte Dunki, 153 USPQ 678 (Bd. App. 1967) and Clinical Products, Ltd. v. Brenner, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). Applicant is directed to cancel the claim or amend it so that resides clearly within one of the statutory classes for examination.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8-13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Avital et al.,("charcoal is a Sensitive, Specific, and stable Marker for the Diagnostic of Aspiration in Hamsters", Pediatric Research, March 2002, pp. 397-401, Vol. 51, No. 3,) cited in the 892 form in view of and Joon et al. (Assessment of Biodegradability of polymeric Microspheres in vivo: Poly(DL-lactic acic), and poly(L-lactic acid) and poly(DL-lactide-co-glycolide)

microspheres, Arch. Pharm. Res. Vol 16, No. 4, pp. 312-317, 1193"), cited in the 892 form .

The instant claims are drawn to a method of detecting of detecting pulmonary aspiration or gastroesophagal reflux comprising administering to subject biodegradable polymeric microspheres, obtaining broncholalveolar lavage and detecting the presence of said microspheres within alveolar macrophages.

As to claims 8 and 9, Avitar et al. teaches a diagnostic composition for detecting aspiration by Instillation of charcoal particles in trachea of hamsters. Instillation of activated charcoal particles mixed with milk was compared with instillation of normal saline or milk in hamsters and the charcoal particles were identified in bronchoalveolar lavage fluid and alveolar macrophages for a period of 3 months. The charcoal particles were made from an inert non-harmful material and are used as a sensitive, specific and stable marker for the diagnosis of aspiration (page 397, right column). Avital et al. also teaches that aspiration can occur in children with neurologic impairment, but can be secondary to gastroesophaageal reflux and the administration of the charcoal particles can be given orally (page 397, left column). Furthermore, Avital et al teaches charcoal particles are too large and may retain within the lungs tissue for extended periods and behave as foreign bodies, inducing chronic inflammatory response and may not be safe as a diagnostic tool for humans (last 3 lines, right column, page 400 and 401 bridging).

Avital et al does not teach a diagnostic composition comprising administering biodegradable polyester microspheres (polylactic acid) having 0.1-10 microns, but suggests that particles that are small in size, inert, non-harmful and can be retained in the lungs tissue safely for extended period could help in the diagnosis of aspiration.

As to claims 10-13 and 15, Joon teaches non toxic, non-tissue reactive biocompatible and biodegradable polyester microspheres such as PDLA poly(Dl-lactic acid), PLLA poly(L-lactic acid) and PLGA poly(DL-lactide-co-glycolide) selected as model polymers as noble drug carriers of various drugs and their biodegradability was determined by analysis of magnetite content in the microspheres (page 312, second paragraph, right column). 3.93 microns-5.52 microns of the polyester microspheres were administered to mice and retained in their lungs (page 313, animal experiments). Particles ranging from 3 to 6 microns were mainly accumulated in the lungs and liver (page 314, second paragraph left column), due to their slow degradation (page 314, first paragraph, right column). The biodegradation of the copolymers is a function of the composition of lactic acid and glycolic acid. The recovery of the microspheres in the lungs was achieved by a magnet (page 316, first paragraph, left column).

Therefore, It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the Avital' s reference with that of Joon to administer an inert and non-harmful material, such as polyester microspheres

as demonstrated by Avital in view of Joon, that can be retained in the lungs by inherent ingestion of alveolar macrophage for the detection of pulmonary aspiration having small and uniform particle size.

Although, Joon utilizes a magnet as a method of detection, however one of ordinary skill in the art would have recognized that other techniques such as broncholaveolar lavage would have also been able to perform the same task once the skill artisan in the art realizes polyester microspheres particles can be retained in the lungs, because Avital suggests obtaining bronchoalveolar lavage and detecting the presence small, inert and non-harmful particles that can be retained in the lungs is a technique that has been used for the detection of particles in the lungs.

Because of the supporting properties of polyester microspheres, the scope of the claims is embraced by the teaching of the cited references.

One would have been motivated to do so; with a reasonable expectation of success to substitute the polyester microspheres as a sensitive and specific marker that could help diagnose aspiration, because they are safe, nonharmful, biodegradable and reliable. The techniques and skill required for making such substitution is conventional knowledge or well within the skill of ordinary artisan as microspheres have been used for a long time. One would have been motivated to combine the references and make the substitution because they are drawn to the same technical filed (constituted with the

same ingredients and share common utilities, and pertinent to the problem which applicant concerns about./ MPEP 2141.01 (a).

All the critical elements required by the claims are obvious over the well taught and thus, the claimed subject matter is not patentably distinct over the prior art of the invention.

In conclusion

8. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEAN CORNET whose telephone number is (571)270-7669. The examiner can normally be reached on Monday-Friday 7.00am-5.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JC/

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614